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Research Forecast and Progress Report

Grant Number: AFOSR-84-0213

Grant Title: Analysis and Synthesis of Adaptive Neural Elements

Period of Report: 1 August 1984 through 30 April 1985

During the period between 01 August 1984 and 30 April 1985 progress on the proposal entitled "Analysis and synthesis of adaptive neural networks" has been in two major directions. First, we have performed experimental studies on the modulation of ionic conductance mechanisms in individual neurons that are believed to contribute to neuronal plasticity and learning. Second, we have begun to develop a single-cell neuronal model for associative learning and simulated the initial model on a digital computer. Progress in each area is described below.

A. Analysis of an ionic conductance mechanism contributing to associative and nonassociative neuronal modifications.

Initially, progress was slow due to delays in recruiting a suitable Senior Research Associate and delays in receiving the electrophysiological equipment necessary to perform the experiments. While all the equipment has still not arrived and a complete rig is unavailable, experiments have begun using another rig in the laboratory that has become available for an interim period. Dr. Douglas Baxter, formally a postdoctoral fellow with Dr. Thomas Brown at the City of Hope Research Institute, joined the project on 14 January, 1985. While just getting started, Dr. Baxter has made remarkable progress in learning the experimental techniques and has begun to collect useful data. Dr. Baxter is examining how ionic conductances are modulated in individual sensory neurons in response to the type of modulatory input that occurs during learning. The eventual goal is to formulate a complete quantitative description of the underlying biochemical and biophysical processes that will be used for our computer simulations (see below). The modulatory input to the sensory neurons acts by increasing the



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levels of intracellular cyclic AMP. Previously, the changes in levels of cyclic AMP were thought to regulate a single type of ion channel. Dr. Baxter's preliminary results indicate that two different channels may be regulated. Further analysis of these modulatory effects as well as their physiological significance is currently in progress.

B. Computer simulation of associative neuronal modifications

Progress was initially slow due to delays in recruiting a computer programmer but now a suitable individual has been hired and we are beginning to make substantial progress. Our goal in these studies is to model and simulate various learning phenomena based on information derived from studies of basic subcellular processes regulating neuronal function and plasticity. The data for the model is obtained from our own experimental work (see above) as well as from the literature.

The starting point for these studies was a neuronal model of simple nonassociative forms of synaptic plasticity that was recently developed by Gingrich and Byrne (J. Neurophysiol. 53:652-669, 1985). As part of the current project this model has been expanded and refined. As a result we are now on the verge of having available for the first time a single-cell neuronal model for associative learning that is based on modern cell biological principles. The model was constructed in order to fit the experimental data of Walters and Byrne (Science 219:405-408, 1983). While still being refined, the model accounts for this data. In addition, it successfully predicts phenomena that were not considered during its construction. For example, it is capable of generating an interstimulus interval (ISI) function curve for classical conditioning similar to that obtained from behavioral studies both in Aplysia and other animals, including man. In the model the

strength of an association is dependent upon the levels of intracellular calcium concentration (caused by the CS) at the time the unconditioned stimulus is applied. The ISI function curve can be explained in terms of the time-course of intracellular calcium regulation.

C. Plans for the Future

Experiments will proceed as outlined in the original proposal. Progress is being made and there seems no reason to change the research plans at this time. As experimental data accumulate, Dr. Baxter will begin to interface to a greater extent with the simulation aspects of the proposal in order to further refine the neuronal model and base it to a greater extent on our own experimental data.

The computer simulations will continue and be expanded. Our current model simulates a nerve action potential with a simple rectangular pulse. This pulse approximation will be replaced with a Hodgkin-Huxley type membrane model which is considerably more physiological. Dr. Baxter will help obtain the necessary parameter estimates for the Hodgkin-Huxley model from his voltage-clamp experiments. Finally, the current single-cell model will be expanded into a network model and emergent adaptive properties of the system will be analyzed.